PROC (BAYL UNIV MED CENT)
2019;32(3):425–426

https://doi.org/10.1080/08998280.2019.1618659

Taylor & Francis
Taylor & Francis Group

Baclofen-induced toxicity in renal disease with neurotoxicity and skin rash

Lakshmi Kant Pathak, MD[a], Ambarish Athavale, MD[b], and Ian Martinez, MD[c]

[a]Department of Nephrology, University of Illinois at Chicago, Chicago, Illinois; [b]Department of Nephrology, Cook County Health and Hospital System, Chicago, Illinois; [c]Department of Medicine, Cook County Health and Hospital System, Chicago, Illinois

ABSTRACT

Baclofen is approved by the Food and Drug Administration for spasticity and is also used off-label for trigeminal neuralgia, cluster headache, and substance abuse dependency. Baclofen is 90% renally excreted and has a variable threshold for toxicity in patients with chronic kidney disease. We present a case of accidental overdose of baclofen in a 58-year-old woman with intractable trigeminal neuralgia. She presented with baclofen neurotoxicity symptoms including confusion and tremors and had a morbilliform rash in the dorsum of both hands. This simultaneous presentation is rare and has never been reported. Her symptoms resolved after hemodialysis treatment.

KEYWORDS Baclofen toxicity; morbilliform rash; neurotoxicity

Baclofen is a gamma-aminobutyric acid agonist that was approved by the US Food and Drug Administration for muscle spasticity in the 1970s. It is used off-label for intractable hiccups, trigeminal neuralgia, cluster headache, and substance abuse from alcohol and cocaine dependency. Baclofen is primarily excreted by the kidneys in its unchanged form and therefore there is a risk of developing toxicities in patients with chronic kidney disease. We present a case of simultaneous neurologic and dermatologic toxicity due to baclofen overdose in a patient with end-stage renal disease (ESRD).

CASE REPORT

A 58-year-old Hispanic woman with ESRD on hemodialysis, with hypertension, type 2 diabetes, and refractory trigeminal neuralgia, was prescribed carbamazepine 200 mg twice a day along with 2.5 mg baclofen twice a day for intractable facial pain. Her daughter misunderstood the dose indication and gave her a higher dose (a full 10-mg tablet instead of one-fourth of a 10-mg tablet). The next day the patient developed altered mental status (repeating the same words) and drowsiness. She also developed multiple episodes of emesis, progressive confusion, and morbilliform rash in both hands *(Figure 1)* and was brought to the emergency department for evaluation.

On admission she was found to be drowsy but arousable, oriented only to person, with hyporeflexia, hypotonia, and tremors in her extremities. Laboratory analysis showed a glucose level of 233 mg/dL; blood urea nitrogen, 79 mg/dL; creatinine, 8.7 mg/dL; hemoglobin, 11.6 g/dL; and phosphate, 5.2 mg/dL. The other results of the complete blood count and basic metabolic panel were unremarkable. Urine drug screen for alcohol and drug abuse was negative. Serial head computed tomography scans showed no signs of any intracranial pathology. Infectious workup including blood cultures was negative. Baclofen toxicity was suspected as a temporal cause based on the presentation, and levels were elevated at 0.41 μg/mL (normal <0.02).

Baclofen was discontinued, and emergent hemodialysis was performed with rapid improvement in mental status, morbilliform rash, hyporeflexia, and tremors after two sessions of 4-hour hemodialysis on two consecutive days. The patient's mental status returned to normal and her skin rash resolved; she was discharged home after 3 days.

DISCUSSION

This case illustrates an extremely rare simultaneous appearance of morbilliform rash and neurotoxicity in a patient after baclofen overdose. After oral consumption, baclofen is rapidly absorbed by the first part of the small

Corresponding author: Lakshmi Kant Pathak, MD, Department of Nephrology, University of Illinois at Chicago, 820 S. Wood St., Chicago, IL 60612 (e-mail: lpatha2@uic.edu)
Received February 22, 2019; Revised May 5, 2019; Accepted May 9, 2019.

Figure 1. Morbilliform rash involving the forearm and hand.

intestine. Peak concentrations are seen in plasma after 2 hours of ingestion. Approximately 10% to 15% of the drug undergoes hepatic metabolism, and the remaining 85% to 90% is excreted unchanged by the kidneys. Baclofen drug clearance follows first-order elimination kinetics with a half-life of 3.5 to 6 hours in patients with normal renal function.[1] However, the pharmacokinetics data in patients with chronic kidney disease are not predictable, and dosage recommendations remain empirical.[2]

The adverse effects associated with baclofen are consistent with its inhibitory effect on the central nervous system. Common side effects include transient drowsiness, lethargy, nausea, and orthostatic signs. Larger doses can cause central nervous system depression, which manifests as sedation, areflexia, somnolence, respiratory depression, and coma requiring intubation.[3]

In very rare cases, toxicity can present as a morbilliform rash that tends to improve with withdrawal of the medication. In a published series of four cases, patients who were treated with baclofen for alcohol dependence developed a morbilliform rash at different treatment doses, indicating that the rash was dose independent and an idiosyncratic reaction.[4] Baclofen has a low molecular weight, low volume distribution, and low protein binding capacity, making it easy to dialyze. Although the percentage of clearance varies with each person and the duration of hemodialysis session, it can be up to 79% cleared in one treatment session, with rapid neurological improvement after two sessions.[5]

Currently, there are no clear guidelines for dosing of baclofen in patients with ESRD. In view of unpredictable pharmacokinetics, dose recommendations and titrations should be done cautiously in patients with advanced chronic kidney disease or on dialysis.

ORCID

Ian Martinez http://orcid.org/0000-0003-2397-6981

1. Gerkin R, Curry SC, Vance MV, Sankowski PW, Meinhart RD. First-order elimination kinetics following baclofen overdose. *Ann Emerg Med.* 1986;15:843–846.
2. Vlavonou R, Perreault MM, Barrière O, et al. Pharmacokinetic characterization of baclofen in patients with chronic kidney disease: dose adjustment recommendations. *J Clin Pharmacol.* 2014;54:584–592. doi:10.1002/jcph.247.
3. Wolf E, Kothari NR, Roberts JK, Sparks MA. Baclofen toxicity in kidney disease. *Am J Kidney Dis.* 2018;71:275–280. doi:10.1053/j.ajkd.2017.07.005.
4. Saddichha S, Jayaram N, Manjunatha N, et al. Baclofen-induced morbiliform rashes: a case series. *J Clin Pharmacol.* 2011;51:1733–1734. doi:10.1177/0091270010385936.
5. Wu VC, Lin SL, Lin SM, Fang CC. Treatment of baclofen overdose by haemodialysis: a pharmacokinetic study. *Nephrol Dial Transplant.* 2005;20:441–443. doi:10.1093/ndt/gfh297.